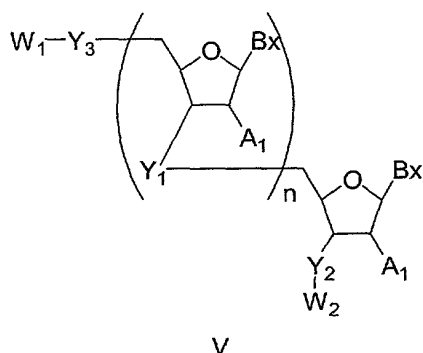


## WHAT IS CLAIMED IS:

1. An oligomeric compound of formula V:



- 5 wherein:

n is from 3 to about 50;

each Y<sub>1</sub> is, independently, an internucleoside linking group;

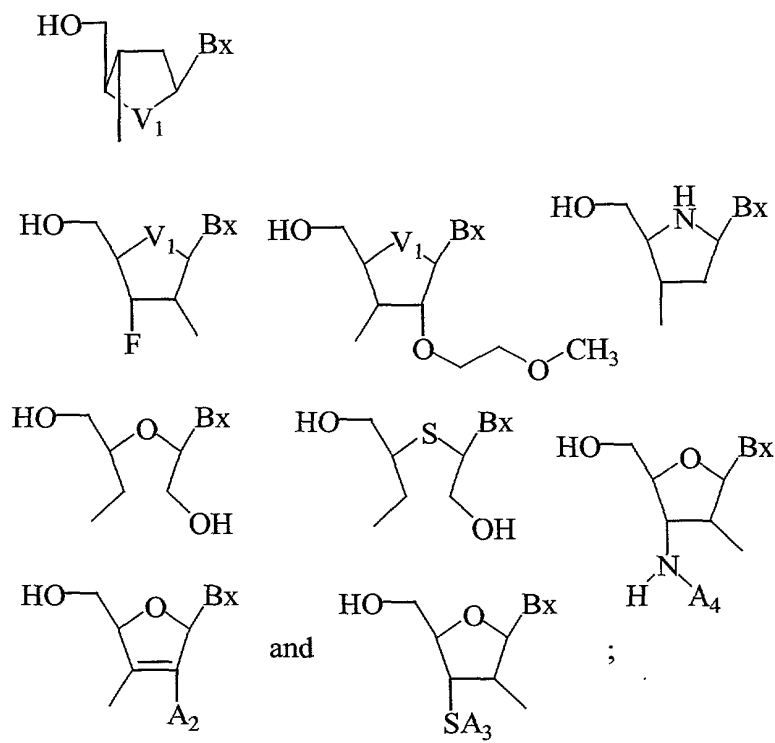
Y<sub>2</sub> is oxygen or an internucleoside linking group;

Y<sub>3</sub> is oxygen or an internucleoside linking group;

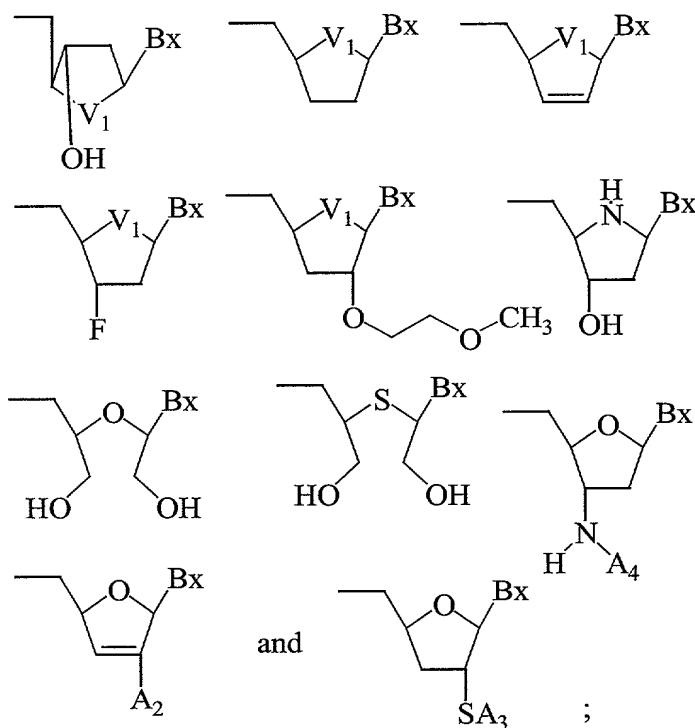
- 10 each Bx is an optionally protected heterocyclic base moiety;

each A<sub>1</sub> is, independently, hydrogen or a sugar substituent group;

$W_1$  is hydrogen, a hydroxyl protecting group or a modified nucleoside selected from the group consisting of



W<sub>2</sub> is hydrogen, a hydroxyl protecting group or a modified nucleoside selected from the group consisting of



5

each A<sub>2</sub> is, independently, alkyl, alkenyl, alkynyl, aryl, alkaryl, O-alkyl, O-aryl, amino, substituted amino, -SH, -SA<sub>3</sub>, thioether, F, or morpholino;

each A<sub>3</sub> is, independently, H, a sulfur protecting group, aryl, alkaryl, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, or alkaryl, wherein said substitution is OA<sub>5</sub> or SA<sub>5</sub>;

each A<sub>4</sub> is, independently, H, a nitrogen protecting group, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted or unsubstituted C<sub>2</sub>-C<sub>10</sub> alkynyl, or alkaryl, wherein said substitution is OA<sub>5</sub> or SA<sub>5</sub>;

each A<sub>5</sub> is, independently, hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl, cycloalkyl or aryl;

each V<sub>1</sub> is, independently, O or S;

wherein at least one of W<sub>1</sub> and W<sub>2</sub> is not hydrogen or a hydroxyl protecting group and at least one internucleoside linking group is not a phosphodiester linking group.

20

2. The oligomeric compound of claim 1 wherein n is from about 8 to about 30.

3. The oligomeric compound of claim 1 wherein n is from about 15 to about 25.

5 4. The oligomeric compound of claim 1 wherein each of said internucleoside linking groups is a phosphorus containing internucleoside linking group.

10 5. The oligomeric compound of claim 4 wherein each of said phosphorus containing internucleoside linking groups is independently selected from the group consisting of phosphodiester, phosphorothioate, chiral phosphorothioate, phosphorodithioate, phosphotriester, aminoalkylphosphotriester, methyl phosphonate, alkyl phosphonate, 5'-alkylene phosphonate, chiral phosphonate, phosphinate, phosphoramidate, 3'-amino phosphoramidate, aminoalkylphosphoramidate, thionophosphoramidate, thionoalkylphosphonate, thionoalkylphosphotriester, 15 selenophosphate and boranophosphate.

6. The oligomeric compound of claim 5 wherein none of said internucleoside linking groups is a phosphodiester internucleoside linking group.

20 7. The oligomeric compound of claim 5 wherein greater than 90% of said internucleoside linking groups are phosphorothioate internucleoside linking groups.

8. The oligomeric compound of claim 1 wherein at least one of said internucleoside linking groups is a non-phosphorus containing internucleoside linking 25 group.

9. The oligomeric compound of claim 8 wherein greater than 90% of said internucleoside linking groups are non-phosphorus containing internucleoside linking groups.

30 10. The oligomeric compound of claim 9 wherein each of said non-phosphorus containing internucleoside linking groups is, independently, selected from the group consisting of morpholino, siloxane, sulfide, sulfoxide, sulfone, formacetyl,

thioformacetyl, methylene formacetyl, thioformacetyl, sulfamate, methyleneimino, methylenehydrazino, sulfonate, sulfonamide, and amide.

11. The oligomeric compound of claim 10 wherein each of said internucleoside  
5 linking groups is, independently,  $-\text{CH}_2\text{-NH-O-CH}_2-$ ,  $-\text{CH}_2\text{-N(CH}_3\text{)-O-CH}_2-$  or  $-\text{CH}_2\text{-O-N(CH}_3\text{)-CH}_2-$ ,  $-\text{CH}_2\text{-N(CH}_3\text{)-N(CH}_3\text{)-CH}_2-$  or  $-\text{O-N(CH}_3\text{)-CH}_2\text{-CH}_2-$ .

12. The oligomeric compound of claim 1 wherein said oligomeric compound is a  
gapmer, hemimer or inverted gapmer.

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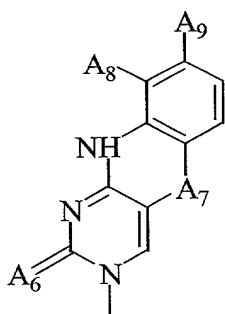
13 The oligomeric compound of claim 12 comprising at least one  $2'\text{-O-CH}_2\text{CH}_2\text{-O-CH}_3$  sugar substituent group in at least one region of said gapmer, hemimer or inverted gapmer.

15

14. The oligomeric compound of claim 1 comprising at least one nucleoside wherein Bx is a polycyclic heterocyclic base moiety.

15. The oligomeric compound of claim 14 wherein each of said polycyclic heterocyclic base moieties is, independently, of the formula:

20



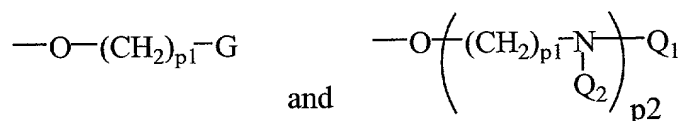
wherein

A<sub>6</sub> is O or S;

25

A<sub>7</sub> is CH<sub>2</sub>, N-CH<sub>3</sub>, O or S;

each A<sub>8</sub> and A<sub>9</sub> is hydrogen or one of A<sub>8</sub> and A<sub>9</sub> is hydrogen and the other of A<sub>8</sub> and A<sub>9</sub> is selected from the group consisting of



wherein:

G is -CN, -OA<sub>10</sub>, -SA<sub>10</sub>, -N(H)A<sub>10</sub>, -ON(H)A<sub>10</sub> or -C(=NH)N(H)A<sub>10</sub>;

Q<sub>1</sub> is H, -NHA<sub>10</sub>, -C(=O)N(H)A<sub>10</sub>, -C(=S)N(H)A<sub>10</sub> or -

5 C(=NH)N(H)A<sub>10</sub>,

each Q<sub>2</sub> is, independently, H or Pg;

A<sub>10</sub> is H, Pg, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, acetyl, benzyl, -(CH<sub>2</sub>)<sub>p3</sub>NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>p3</sub>N(H)Pg, a D or L α-amino acid, or a peptide derived from D, L or racemic α-amino acids;

10 Pg is a nitrogen, oxygen or thiol protecting group;

each p<sub>1</sub> is, independently, from 2 to about 6;

p<sub>2</sub> is from 1 to about 3; and

p<sub>3</sub> is from 1 to about 4.

15 16. The oligomeric compound of claim 1 wherein Y<sub>3</sub> is an internucleoside linking group and W<sub>1</sub> is a modified nucleoside.

17. The oligomeric compound of claim 1 wherein Y<sub>2</sub> is an internucleoside linking group and W<sub>2</sub> is a modified nucleoside.

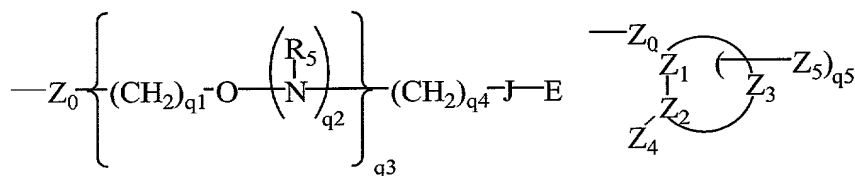
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18. The oligomeric compound of claim 1 wherein each of said B<sub>x</sub> is independently selected from the group consisting of adeninyl, guaninyl, thyminyl, cytosinyl, uracilyl, 5-methylcytosinyl (5-me-C), 5-hydroxymethyl cytosinyl, xanthinyl, hypoxanthinyl, 2-aminoadeninyl, alkyl derivatives of adeninyl and  
 25 guaninyl, 2-thiouracilyl, 2-thiothyminyl, 2-thiocytosinyl, 5-halouracilyl, 5-halocytosinyl, 5-propynyl uracilyl, 5-propynyl cytosinyl, 6-azo uracilyl, 6-azo cytosinyl, 6-azo thyminyl, 5-uracilyl (pseudouracil), 4-thiouracilyl, 8-substituted adeninyls and guaninyls, 5-substituted uracilyls and cytosinyls, 7-methylguaninyl, 7-methyladeninyl, 8-azaguaninyl, 8-azaadeninyl, 7-deazaguaninyl, 7-deazaadeninyl, 3-  
 30 deazaguaninyl and 3-deazaadeninyl.

19. The oligomeric compound of claim 1 wherein each sugar substituent group is, independently, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>5</sub>-C<sub>20</sub> aryl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-alkylamino, -O-alkylalkoxy, -O-alkylaminoalkyl, -O-alkylimidazole, -OH, -SH, -S-alkyl, -S-alkenyl, -S-alkynyl, -N(H)-alkyl, -N(H)-alkenyl, -N(H)-alkynyl, -N(alkyl)<sub>2</sub>, -O-aryl, -S-aryl, -NH-aryl, -O-aralkyl, -S-aralkyl, -N(H)-aralkyl, phthalimido (attached at N), halogen, amino, keto (-C(=O)-R), carboxyl (-C(=O)OH), nitro (-NO<sub>2</sub>), nitroso (-N=O), cyano (-CN), trifluoromethyl (-CF<sub>3</sub>), trifluoromethoxy (-O-CF<sub>3</sub>), imidazole, azido (-N<sub>3</sub>), hydrazino (-N(H)-NH<sub>2</sub>), aminooxy (-O-NH<sub>2</sub>), isocyanato (-N=C=O), sulfoxide (-S(=O)-R), sulfone (-S(=O)<sub>2</sub>-R), disulfide (-S-S-R), silyl, heterocyclyl, carbocyclyl, an intercalator, a reporter group, a conjugate group, polyamine, polyamide, polyalkylene glycol or a polyether of the formula (-O-alkyl)<sub>m</sub>, where m is 1 to about 10;

wherein each R is, independently, hydrogen, a protecting group or substituted or unsubstituted alkyl, alkenyl, or alkynyl wherein the substituent groups are selected from haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy or aryl as well as halogen, hydroxyl, amino, azido, carboxy, cyano, nitro, mercapto, a sulfide group, a sulfonyl group and a sulfoxide group;

or each sugar substituent group has one of formula I or II:



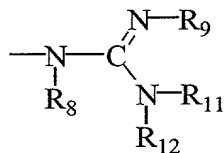
wherein:

Z<sub>0</sub> is O, S or NH;

J is a single bond, O or C(=O);

E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(R<sub>5</sub>)(R<sub>6</sub>), N(R<sub>5</sub>)(R<sub>7</sub>), N=C(R<sub>5a</sub>)(R<sub>6a</sub>), N=C(R<sub>5a</sub>)(R<sub>7a</sub>) or has

formula III;



III

each  $R_8$ ,  $R_9$ ,  $R_{11}$  and  $R_{12}$  is, independently, hydrogen,  $C(O)R_{13}$ , substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally,  $R_{11}$  and  $R_{12}$ , together form a phthalimido moiety with the nitrogen atom to which they are attached;

each  $R_{13}$  is, independently, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, trifluoromethyl, cyanoethoxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

$R_5$  is hydrogen, a nitrogen protecting group or -T-L,

$R_{5a}$  is hydrogen, a nitrogen protecting group or -T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a solid support medium;

each  $R_6$  and  $R_7$  is, independently, H, a nitrogen protecting group, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, alkynyl;  $NH_3^+$ ,  $N(R_{14})(R_{15})$ , guanidino and acyl where said acyl is an acid amide or an ester;

or  $R_6$  and  $R_7$ , together, are a nitrogen protecting group, are joined in a ring structure that optionally includes an additional heteroatom selected from N and O or are a chemical functional group;

each  $R_{14}$  and  $R_{15}$  is, independently, H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{14}$  and  $R_{15}$ , together, are a nitrogen protecting group;

or  $R_{14}$  and  $R_{15}$  are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

$Z_4$  is OX, SX, or  $N(X)_2$ ;

each X is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)R_{16}$ ,  $C(=O)N(H)R_{16}$  or  $OC(=O)N(H)R_{16}$ ;

$R_{16}$  is H or  $C_1$ - $C_8$  alkyl;



Z<sub>1</sub>, Z<sub>2</sub> and Z<sub>3</sub> comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms wherein said heteroatoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated

5 heterocyclic;

Z<sub>5</sub> is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(R<sub>5</sub>)(R<sub>6</sub>) OR<sub>5</sub>, halo, SR<sub>5</sub> or CN;

each  $q_1$  is, independently, an integer from 1 to 10;

10 each  $q_2$  is, independently, 0 or 1;

$q_3$  is 0 or an integer from 1 to 10;

$q_4$  is an integer from 1 to 10;

$q_5$  is from 0, 1 or 2; and

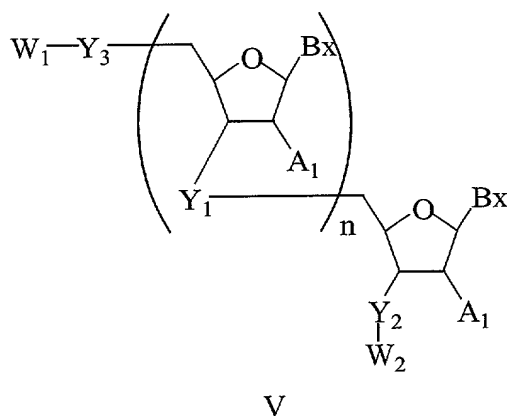
provided that when  $q_3$  is 0,  $q_4$  is greater than 1.

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20. The oligomeric compound of Claim 19 wherein each of said sugar substituent groups is, independently,  $-\text{O}-\text{CH}_2\text{CH}_2\text{OCH}_3$ ,  $-\text{O}(\text{CH}_2)_2\text{ON}(\text{CH}_3)_2$ ,  $-\text{O}-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-\text{N}(\text{CH}_3)_2$ ,  $-\text{O}-\text{CH}_3$ ,  $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ ,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ , or fluoro.

20

21. A method of enhancing the nuclease resistance of an oligomeric compound comprising providing at least one modified nucleoside at either the 3' or 5' terminus of said oligomeric compound to give a modified oligomeric compound of formula V:



25 wherein:

n is from 3 to about 50;

each  $Y_1$  is, independently, an internucleoside linking group;

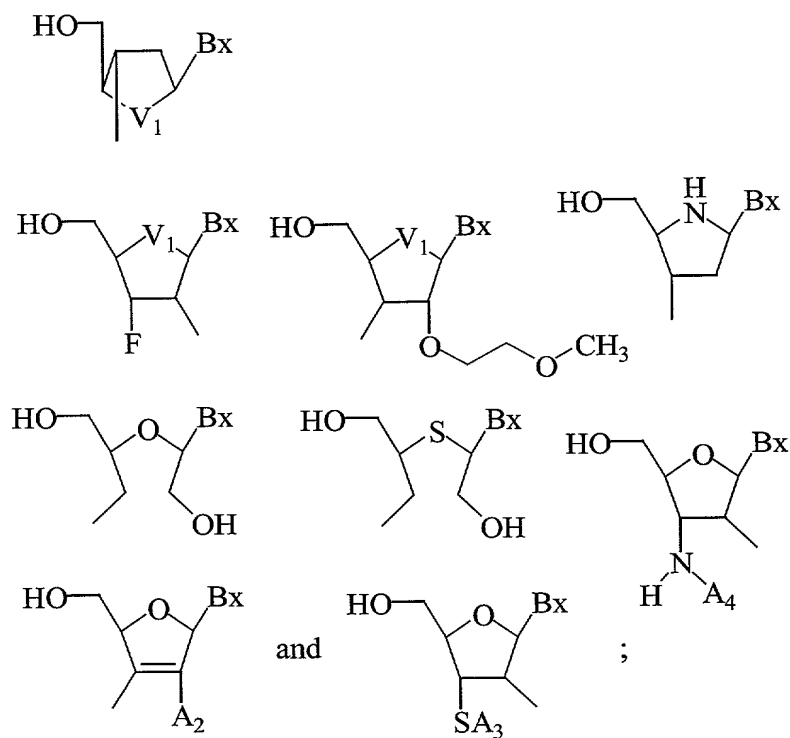
$Y_2$  is oxygen or an internucleoside linking group;

$Y_3$  is oxygen or an internucleoside linking group;

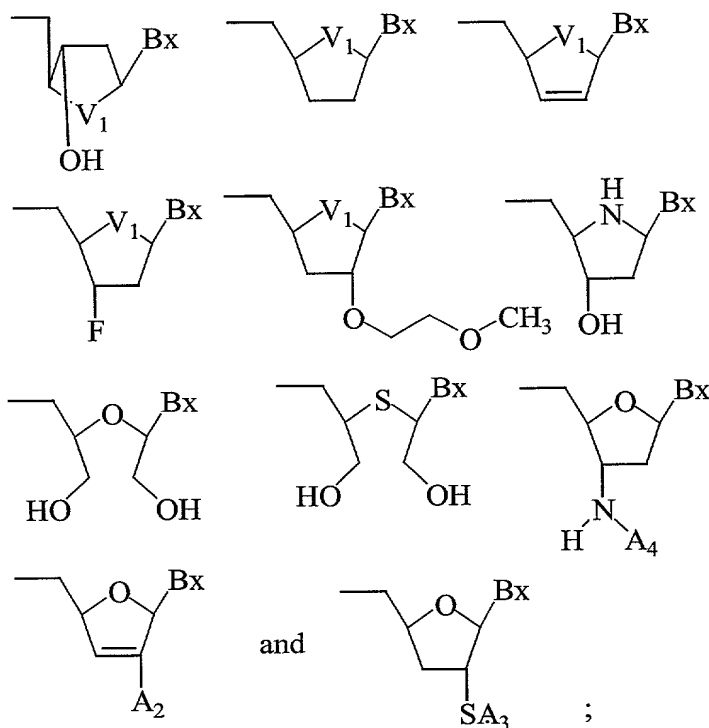
each  $Bx$  is an optionally protected heterocyclic base moiety;

5 each  $A_1$  is, independently, hydrogen or a sugar substituent group;

$W_1$  is hydrogen, a hydroxyl protecting group or a modified nucleoside selected from the group consisting of



$W_2$  is hydrogen, a hydroxyl protecting group or a modified nucleoside selected from the group consisting of



5

each  $A_2$  is, independently, alkyl, alkenyl, alkynyl, aryl, alkaryl, O-alkyl, O-aryl, amino, substituted amino,  $-SH$ ,  $-SA_3$ , thioether,  $F$ , or morpholino;

each  $A_3$  is, independently,  $H$ , a sulfur protecting group, aryl, alkaryl, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, or alkaryl, wherein said substitution is  $OA_5$  or  $SA_5$ ;

each  $A_4$  is, independently,  $H$ , a nitrogen protecting group, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, or alkaryl, wherein said substitution is  $OA_5$  or  $SA_5$ ;

each  $A_5$  is, independently, hydrogen,  $C_1$ - $C_{10}$  alkyl, cycloalkyl or aryl;

each  $V_1$  is, independently,  $O$  or  $S$ ;

wherein at least one of  $W_1$  and  $W_2$  is not hydrogen or a hydroxyl protecting group.

20

22. The method of claim 21 wherein n is from about 8 to about 30.

23. The method of claim 21 wherein n is from about 15 to about 25.

5 24. The method of claim 21 wherein each of said internucleoside linking groups is a phosphorus-containing internucleoside linking group.

25. The method of claim 24 wherein each of said phosphorus containing  
internucleoside linking groups is selected from the group consisting of  
10 phosphodiester, phosphorothioate, chiral phosphorothioate, phosphorodithioate,  
phosphotriester, aminoalkylphosphotriester, methyl phosphonate, alkyl phosphonate,  
5'-alkylene phosphonate, chiral phosphonate, phosphinate, phosphoramidate, 3'-  
amino phosphoramidate, aminoalkylphosphoramidate, thionophosphoramidate,  
thionoalkylphosphonate, thionoalkylphosphotriester, selenophosphate and  
15 boranophosphate.

26. The method of claim 25 wherein none of said internucleoside linking groups is a phosphodiester internucleoside linking group.

20 27. The method of claim 25 wherein greater than 90% of said internucleoside linking groups are phosphodiester internucleoside linking groups.

28. The method of claim 21 wherein at least one of said internucleoside linking groups is a non-phosphorus containing internucleoside linking group.

25

29. The method of claim 28 wherein greater than 90% of said internucleoside linking groups are non-phosphorus containing internucleoside linking groups.

30. The method of claim 29 wherein each of said non-phosphorus containing  
30 internucleoside linking groups is, independently, selected from the group consisting of  
morpholino, siloxane, sulfide, sulfoxide, sulfone, formacetyl, thioformacetyl,  
methylene formacetyl, thioformacetyl, sulfamate, methyleneimino,  
methylenehydrazino, sulfonate, sulfonamide, and amide.

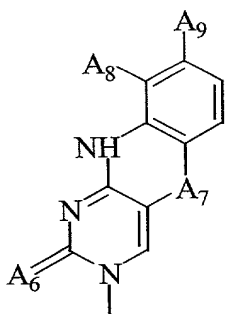
31. The method of claim 30 wherein each of said internucleoside linking groups is, independently,  $-\text{CH}_2-\text{NH}-\text{O}-\text{CH}_2-$ ,  $-\text{CH}_2-\text{N}(\text{CH}_3)-\text{O}-\text{CH}_2-$ ,  $-\text{CH}_2-\text{O}-\text{N}(\text{CH}_3)-\text{CH}_2-$ ,  $-\text{CH}_2-\text{N}(\text{CH}_3)-\text{N}(\text{CH}_3)-\text{CH}_2-$  or  $-\text{O}-\text{N}(\text{CH}_3)-\text{CH}_2-\text{CH}_2-$ .

5 32. The method of claim 21 wherein said oligomeric compound is a gapmer, hemimer or inverted gapmer.

33. The method of claim 32 wherein the oligomeric compound comprises at least one  $2'-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-\text{CH}_3$  sugar substituent group in at least one region of said  
10 gapmer, hemimer or inverted gapmer.

34. The method of claim 21 comprising at least one nucleoside wherein Bx is a polycyclic heterocyclic base moiety.

15 35. The method of claim 34 wherein each of said polycyclic heterocyclic base moieties is, independently, of the formula:



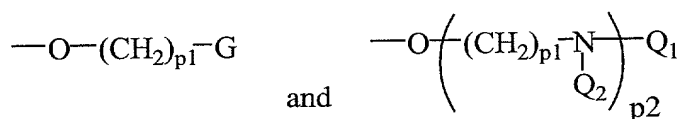
20 wherein

$A_6$  is O or S;

$A_7$  is  $\text{CH}_2$ ,  $\text{N}-\text{CH}_3$ , O or S;

each  $A_8$  and  $A_9$  is hydrogen or one of  $A_8$  and  $A_9$  is hydrogen and the other of  $A_8$  and  $A_9$  is selected from the group consisting of:

25



wherein:

wherein:

G is -CN, -OA<sub>10</sub>, -SA<sub>10</sub>, -N(H)A<sub>10</sub>, -ON(H)A<sub>10</sub> or -C(=NH)N(H)A<sub>10</sub>;

5 Q<sub>1</sub> is H, -NHA<sub>10</sub>, -C(=O)N(H)A<sub>10</sub>, -C(=S)N(H)A<sub>10</sub> or -C(=NH)N(H)-  
A<sub>10</sub>;

each Q<sub>2</sub> is, independently, H or Pg;

A<sub>10</sub> is H, Pg, substituted or unsubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, acetyl, benzyl,  
-(CH<sub>2</sub>)<sub>p3</sub>NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>p3</sub>N(H)Pg, a D or L α-amino acid, or a peptide derived from D, L  
10 or racemic α-amino acids;

Pg is a nitrogen, oxygen or thiol protecting group;

each p<sub>1</sub> is, independently, from 2 to about 6;

p<sub>2</sub> is from 1 to about 3; and

p<sub>3</sub> is from 1 to about 4.

15 36. The method of claim 21 wherein Y<sub>3</sub> is an internucleoside linking group and  
W<sub>1</sub> is a modified nucleoside.

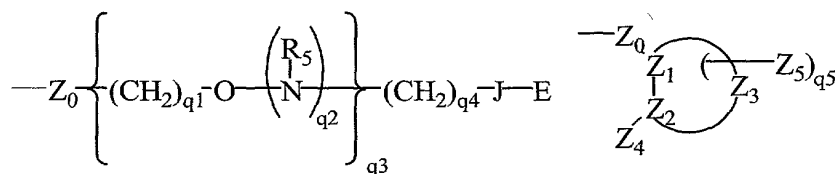
20 37. The method of claim 21 wherein Y<sub>2</sub> is an internucleoside linking group and  
W<sub>2</sub> is a modified nucleoside.

38. The method of claim 21 wherein each of said B<sub>x</sub> is independently selected  
from the group consisting of adeninyl, guaninyl, thyminyl, cytosinyl, uracilyl, 5-  
methylcytosinyl (5-me-C), 5-hydroxymethyl cytosinyl, xanthinyl, hypoxanthinyl, 2-  
25 aminoadeninyl, alkyl derivatives of adeninyl and guaninyl, 2-thiouracilyl, 2-  
thiothyminyl, 2-thiocytosinyl, 5-halouracilyl, 5-halocytosinyl, 5-propynyl uracilyl, 5-  
propynyl cytosinyl, 6-azo uracilyl, 6-azo cytosinyl, 6-azo thyminyl, 5-uracilyl  
(pseudouracil), 4-thiouracilyl, 8-substituted adeninyls and guaninyls, 5-substituted  
uracilyls and cytosinyls, 7-methylguaninyl, 7-methyladeninyl, 8-azaguaninyl, 8-  
30 azaadeninyl, 7-deazaguaninyl, 7-deazaadeninyl, 3-deazaguaninyl and 3-  
deazaadeninyl.

39. The method of claim 21 wherein each sugar substituent group is, independently, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>5</sub>-C<sub>20</sub> aryl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-alkylamino, -O-alkylalkoxy, -O-alkylaminoalkyl, -O-alkylimidazole, -OH, -SH, -S-alkyl, -S-alkenyl, -S-alkynyl, -N(H)-alkyl, -N(H)-alkenyl, -N(H)-alkynyl, -N(alkyl)<sub>2</sub>, -O-aryl, -S-aryl, -NH-aryl, -O-aralkyl, -S-aralkyl, -N(H)-aralkyl, phthalimido (attached at N), halogen, amino, keto (-C(=O)-R), carboxyl (-C(=O)OH), nitro (-NO<sub>2</sub>), nitroso (-N=O), cyano (-CN), trifluoromethyl (-CF<sub>3</sub>), trifluoromethoxy (-O-CF<sub>3</sub>), imidazole, azido (-N<sub>3</sub>), hydrazino (-N(H)-NH<sub>2</sub>), aminooxy (-O-NH<sub>2</sub>), isocyanato (-N=C=O), sulfoxide (-S(=O)-R), sulfone (-S(=O)<sub>2</sub>-R), disulfide (-S-S-R), silyl, heterocyclyl, carbocyclyl, an intercalator, a reporter group, a conjugate group, polyamine, polyamide, polyalkylene glycol or a polyether of the formula (-O-alkyl)<sub>m</sub>, where m is 1 to about 10;

wherein each R is, independently, hydrogen, a protecting group or substituted or unsubstituted alkyl, alkenyl, or alkynyl wherein the substituent groups are selected from haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy or aryl as well as halogen, hydroxyl, amino, azido, carboxy, cyano, nitro, mercapto, a sulfide group, a sulfonyl group and a sulfoxide group;

or each sugar substituent group has one of formula I or II:



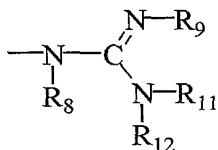
wherein:

Z<sub>0</sub> is O, S or NH;

J is a single bond, O or C(=O);

E is C<sub>1</sub>-C<sub>10</sub> alkyl, N(R<sub>5</sub>)(R<sub>6</sub>), N(R<sub>5</sub>)(R<sub>7</sub>), N=C(R<sub>5a</sub>)(R<sub>6a</sub>), N=C(R<sub>5a</sub>)(R<sub>7a</sub>) or has

formula III;



III

each  $R_8$ ,  $R_9$ ,  $R_{11}$  and  $R_{12}$  is, independently, hydrogen,  $C(O)R_{13}$ , substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally,  $R_{11}$  and  $R_{12}$ , together form a phthalimido moiety with the nitrogen atom to which they are attached;

each  $R_{13}$  is, independently, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, trifluoromethyl, cyanoethyloxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

$R_5$  is hydrogen, a nitrogen protecting group or -T-L,

$R_{5a}$  is hydrogen, a nitrogen protecting group or -T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a solid support medium;

each  $R_6$  and  $R_7$  is, independently, H, a nitrogen protecting group, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkenyl, substituted or unsubstituted  $C_2$ - $C_{10}$  alkynyl, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, alkynyl;  $NH_3^+$ ,  $N(R_{14})(R_{15})$ , guanidino and acyl where said acyl is an acid amide or an ester;

or  $R_6$  and  $R_7$ , together, are a nitrogen protecting group, are joined in a ring structure that optionally includes an additional heteroatom selected from N and O or are a chemical functional group;

each  $R_{14}$  and  $R_{15}$  is, independently, H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{14}$  and  $R_{15}$ , together, are a nitrogen protecting group;

or  $R_{14}$  and  $R_{15}$  are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

$Z_4$  is OX, SX, or  $N(X)_2$ ;

each X is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl,  $C(=NH)N(H)R_{16}$ ,  $C(=O)N(H)R_{16}$  or  $OC(=O)N(H)R_{16}$ ;

$R_{16}$  is H or  $C_1$ - $C_8$  alkyl;



$Z_1$ ,  $Z_2$  and  $Z_3$  comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms wherein said heteroatoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated

5 heterocyclic;

$Z_5$  is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms,  $N(R_5)(R_6)OR_5$ , halo,  $SR_5$  or CN;

each  $q_1$  is, independently, an integer from 1 to 10;

10 each  $q_2$  is, independently, 0 or 1;

$q_3$  is 0 or an integer from 1 to 10;

$q_4$  is an integer from 1 to 10;

$q_5$  is from 0, 1 or 2; and

provided that when  $q_3$  is 0,  $q_4$  is greater than 1.

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40. The method of Claim 39 wherein each of said sugar substituent groups is, independently,  $-O-CH_2CH_2OCH_3$ ,  $-O(CH_2)_2ON(CH_3)_2$ ,  $-O-(CH_2)_2-O-(CH_2)_2-N(CH_3)_2$ ,  $-O-CH_3$ ,  $-OCH_2CH_2CH_2NH_2$ ,  $-CH_2-CH=CH_2$  or fluoro.